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ESTABLISHMENT OF NORMAL ELECTROCARDIOGRAPHIC VALUES FOR RHESUS MONKEYS (Macaca mulatta) UNDER SEDATED AND UNSEDATED CONDITIONS

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SUMMARY PAGE*

THE PROBLEM

To establish normal electrocardiographic values for sedated and unsedated rhesus monkeys housed at Naval Aerospace Medical Research Laboratory.

FINDINGS

Electrocardiographic tracings from 57 female and 56 male rhesus monkeys under sedated and unsedated states were examined to determine normal values for the various parameters. The data were statistically analyzed for significant differences between sex groups and sedated versus unsedated monkeys of the same sex. The results were compared with two previous major electrocardiographic studies on unsedated rhesus monkeys. The P-R interval, QRS duration, and Q-T interval were greater in the NAMRL monkeys. Heart rate and QRS axis were similar to those reported in the two comparison studies.

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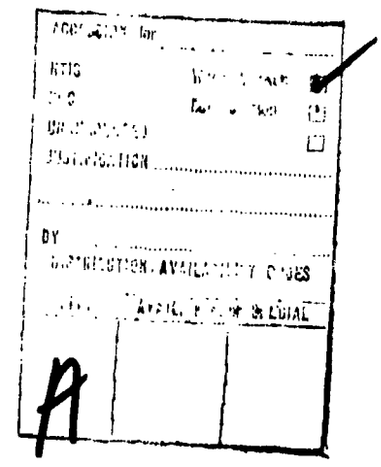

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* The animals used in this study were handled in accordance with the Principles of Laboratory Animal Care established by the Committee on the Guide for Laboratory Animal Resources, National Academy of Science-National Research Council.

INTRODUCTION

A survey of the scientific literature on the electrocardiograms of normal rhesus monkeys (Macaca mulatta) revealed only a few reports (1-3) and one comprehensive review (4). Information available from those studies was of limited value for our purposes due to variations in monkey populations, methods, equipment, and results. Since the electrocardiogram is an essential component of the selection criteria utilized for the Naval Aerospace Medical Research Laboratory (NAMRL) research studies involving the use of rhesus monkeys, it became necessary to establish normal values for the rhesus monkey population at this laboratory.

This report summarizes electrocardiographic data obtained under standardized conditions from 57 female and 56 male rhesus monkeys. Electrocardiograms were recorded from each animal while seated upright in a Plexiglas restraint chair, both under the effects of a neuroleptic-narcotic combination drug,* and in an unmedicated state.

SUBJECTS AND PROCEDURE

The subjects involved in this study were rhesus monkeys purchased as a single shipment of 120 animals from another military research laboratory. The monkeys were maintained for a period of 10 months prior to the study on a commercial laboratory primate chow+ supplemented regularly with fresh apples and oranges. Ages of the monkeys were determined by dentition (5). The males ranged in age from 24 months to 54 months, with an arithmetic mean of 42.2 months and a standard deviation of 5.8 months. Females ranged in age from 24 to 80 months, with a mean of 50.1 months and a standard deviation of 8.8 months.

The males ranged in weight from 3.38 to 8.45 kilograms, with a mean of 5.01 kilograms and a standard deviation of 1.2 kilograms. The females ranged in weight from 3.13 to 6.99 kilograms, with a mean of 4.67 kilograms and a standard deviation of 0.74 kilograms.

The 57 female and 56 male monkeys that received electrocardiograms were given routine physical examinations, and determined to be free of clinical illness or disease at the time of data collection. Seven of the original 120 monkeys were not included in the study due to their illness, disability, or death.

SEDATED MONKEYS

Animals were deprived of food for 17 hours prior to the electrocardiography. Thirty minutes before the recording, the monkeys were administered a neuroleptic-narcotic combination drug, fentanyl-droperidol (Innovar®), at a dosage of 1 cc

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* Innovar, McNeil Laboratories, Fort Washington, PA.

\+ Purina Monkey Chow, Ralston Purina Company, Checkerboard Square, St. Louis, Missouri.

per 40 pounds body weight (1 cc per 18.2 kg body weight) intramuscularly (6). This Innovar dosage was sufficient to produce moderate relaxation in the subjects. The sedated monkeys were then placed upright in a Plexiglas restraint chair specifically modified to facilitate electrocardiography (Figure 1). Flat-plate stainless steel electrodes were attached by straps onto the upper arms and legs and affixed with a commercial electrode jelly* to insure proper electrical conduction. Electrocardiographic leads I, II, III, aVR, aVL, and aVF were recorded on a Hewlett-Packard Model 1514A electrocardiograph at a paper speed of 25 millimeters per second. The machine was calibrated so that a one centimeter stylus deflection equalled a one millivolt amplitude.

UNSEDATED MONKEYS

The subjects were physically captured, restrained, and placed upright in Plexiglas restraint chairs after an 18-hour fast. The monkeys were allowed a 5-minute rest period before the tracings were recorded. The procedure, which follows 4 to 5 months after the initial tests with the monkeys sedated, was otherwise identical to that used for the sedated monkeys.

RESULTS

Parameters of the electrocardiograms were measured by standardized techniques and according to the criteria outlined by Bolton (7). Statistical analyses were performed with the Student's T-tests for differences between means. Tables I and II summarize the measurements of 226 tracings on 113 monkeys by sex group.

ELECTROCARDIOGRAPHIC PARAMETERS

Rhythm: All monkeys examined had normal sinus rhythm.

Heart Rate: The heart rate in sedated and unsedated monkeys did not vary significantly with sex. Within sex groups the heart rate was significantly lower ($P < .0005$) in sedated monkeys than in unsedated animals.

P Wave Duration: The duration of the P wave was greater and more varied in sedated females than in unsedated females ($P < .005$) and was greater for females sedated than male sedated monkeys ($P < .05$).

P Wave Amplitude: The P wave amplitude in millivolts for male monkeys under sedation was significantly lower than for the unsedated male group ($P < .005$). The P wave was significantly higher in sedated females than sedated male monkey ($P < .025$).

P-R Interval: This parameter was similar between sexes and between states of consciousness. The greatest variation occurred within the unsedated female group.

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* Day-Baldwin, Inc., Hillside, New Jersey 07205

Table I

Summary of Electrocardiographic Data for Male Macaca mulatta

	Heart Rate Beats/Min	P Wave Sec	P Wave mV	P-R Interval Sec	QRS Duration Sec	R Wave mV	Q-T Interval Sec	QRS Axis degrees
Unsedated								
Mean	255.3	.041	2.46	.079	.039	8.81	.153	59.1
S.D.	25.4	.008	.62	.009	.008	5.78	.022	54.8
Mean ± 2 S.D.	204.5-306.2	.025-.057	1.22-3.70	.061-.097	.023-.055	-2.75-20.37	.109-.197	-50.5-168.7
Sedated *								
Mean	210.3	.041	2.15	.078	.039	9.10	.185	65.2
S.D.	25.2	.006	.56	.008	.007	5.40	.025	42.1
Mean ± 2 S.D.	159.7-260.7	.029-.053	1.03-3.27	.062-.094	.025-.053	-1.70-19.90	.135-.235	-19.0-149.4

* Innovar: 1cc/40 lb weight (1cc/18.2 kg)

Table II

Summary of Electrocardiographic Data for Female *Macaca mulatta*

	Heart Rate Beats/Min	P Wave Sec	P Wave mV	P-R Interval Sec	QRS Duration Sec	R Wave mV	Q-T Interval Sec	QRS Axis degrees
Unsedated								
Mean	248.9	.039	2.37	.083	.037	9.79	.164	61.3
S.D.	24.9	.007	.64	.019	.009	4.72	.036	31.9
Mean ± 2 S.D.	199.1-298.7	.025-.053	1.09-3.65	.045-.121	.019-.055	.35-19.23	.092-.235	- 2.5-125.2
Sedated*								
Mean	215.7	.044	2.40	.079	.045	9.93	.189	62.2
S.D.	27.0	.011	.71	.011	.014	4.31	.026	30.6
Mean ± 2 S.D.	161.7-269.7	.022-.066	.98-3.82	.057-.101	.017-.073	1.31-18.55	.137-.241	1.0-123.4

* Innovar: 1cc/40 lb weight (1cc/18.2 kg)

Figure 1

Plexiglas Restraint Chair Modified to Facilitate Electrocardiography

QRS Duration: The duration of the QRS complex was longest in the female sedated group of subjects. It was significantly greater in the sedated females than in unsedated females ($P < .0005$), and significantly greater in sedated females versus sedated males ($P < .005$).

R Wave Amplitude: The greatest R wave amplitudes were obtained from the sedated female monkeys. These values for females exceeded those for the males in both states of consciousness; however, the differences were significant only when comparing the sedated males with the sedated females ($P < .05$).

Q-T Interval: The Q-T interval was significantly shorter in the unsedated groups when compared with the sedated monkeys ($P < .0005$). This was probably a reflection of the increased heart rate in the unsedated groups (2). A significant difference also existed between unsedated male and unsedated female monkeys ($P < .05$).

QRS Heart Axis: No significant differences in axis were observed between any of the groups of monkeys studied. The axis varied more in male than in female monkeys.

COMMENT

Table III presents a comparison of data from two other studies on the electrocardiograms of rhesus monkeys with those of our study with unsedated subjects. Mean heart rates were similar. The P-R interval, QRS duration, and Q-T interval were greater in NAMRL Macaca mulatta than in those in the study of Atta and Vanace (1) or Malinow (2). This inconsistency is probably related to the differences in the machine paper speeds utilized for each study. Atta and Vanace recorded tracings at 75 mm/sec, Malinow at 50 mm/sec, and Kupper et al. at 25 mm/sec. We have noted that there is a tendency toward wider measurements of the various electrocardiographic parameters as paper speed decreases. If this inverse relationship is assumed, it helps to explain these variations noted in the three studies compared in Table III. Reported heart rates were comparable in the three study groups. The QRS axis for our monkey populations reveale ' more variability in the male group than in the female group. The QRS axis results of the three studies were similar, but difficult to compare due to variations in reporting of the data.

Table III

Comparison of Electrocardiographic Data for Unsedated Macaca mulatta from Selected Studies

Author	Paper Speed mm/sec	Sex	Heart Rate Beats/min	P-R Interval Sec	QRS Duration Sec	Q-T Interval Sec	QRS Axis degrees
Atta & Vanace[a]	75	Both	160-333 (260)	.047-.100 (.064)	.020-.036 (.027)	.107-.200 (.148)	-41 to + 127 (+55)
Malinow[b]	50	Male	252 ± 42	.07 ± .01	.03 ± .005	-	+50 to + 100 (combined sexes; 83% of population)
	50	Female	258 ± 28	.07 ± .01	.03 ± .008	-	
Kupper et al.[b]	25	Male	255 ± 25	.079 ± .009	.039 ± .007	.153 ± .022	+59 ± 55
	25	Female	249 ± 25	.083 ± .019	.037 ± .009	.154 ± .036	+61 ± 32

a Range; mean values in parentheses.

b Mean ± 1 Standard Deviation unless otherwise noted.

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In an attempt to establish normal electrocardiographic values for sedated and unsedated rhesus monkeys at this laboratory, electrocardiographic tracings from 57 female and 56 male rhesus monkeys under sedated and unsedated states were examined to determine normal values for the various parameters. The data were statistically analyzed for significant differences between sex groups and sedated versus unsedated monkeys of the same sex. The results are compared with two previous major electrocardiographic studies on unsedated rhesus monkeys.

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